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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/563,655

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J. Christopher Anderson

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QUINE INTELLECTUAL PROPERTY LAW GROUP, P.C.

P O BOX 458

ALAMEDA, CA 94501

EXAMINER

GEBREYESUS, KAGNEW H

ART UNIT

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/563,655	<b>Applicant(s)</b> ANDERSON ET AL.	
	<b>Examiner</b> KAGNEW H. GEBREYESUS	<b>Art Unit</b> 1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 13 May 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-26 is/are pending in the application.
- 4a) Of the above claim(s) 1-16 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 17-26 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on 1/5/06 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>9/13/07, 10/9/07</u> .  | 6) <input type="checkbox"/> Other: _____                          |

## DETAILED ACTION

Applicant's election with traverse dated May 13, 2008 is acknowledged. Applicants have elected the invention of Group II comprising claims 17-26 and the species of SEQ ID NO: 15 for prosecution. Claims 1-10, 18-26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to non-elected groups, there being no allowable or linking claims. Claims 27-61 have been cancelled. Claims 17-26 with the species of SEQ ID NO: 15 are present for examination.

Applicants argue that the lack of unity is incorrect because the cited reference, Thorbjarnardottir et al does not teach an orthogonal tRNA. Specifically the response argues:

“...the Requirement's analysis of the possible unifying features of, e.g., claims 1 and 17 as presented in the action omits a fundamental unifying feature of the claimed invention, i.e., that the tRNA be orthogonal to the system at issue. The claims should, accordingly, be rejoined...”

Applicant's argument has been considered but not found persuasive because the disclosure of Thorbjarnardottir et al clearly teaches a tRNA<sup>leu</sup> comprising a suppressor codon. Applicant's specification defines an orthogonal tRNA in paragraph [0031] as follows:

[0031] Orthogonal leucyl-tRNA: As used herein, an orthogonal leucyl-tRNA (leucyl-O-tRNA) is a tRNA that is orthogonal to a translation system of interest, where the tRNA is: (1) identical or substantially similar to a naturally occurring leucyl tRNA, (2) derived from a naturally occurring leucyl tRNA by natural or artificial mutagenesis (3) derived by any process that takes a sequence of a wild-type or mutant leucyl tRNA sequence of (1) or (2) into account, (4)

homologous to a wild-type or mutant leucyl tRNA; (5) homologous to any example tRNA that is designated as a substrate for a leucyl tRNA synthetase in Table 3, or (6) a conservative variant of any example tRNA that is designated as a substrate for a leucyl tRNA synthetase in Table 3. The leucyl tRNA can exist charged with an amino acid, or in an uncharged state. It is also to be understood that a "leucyl-O-tRNA" optionally is charged (aminoacylated) by a cognate synthetase with an amino acid other than leucine. Indeed, it will be appreciated that a leucyl-O-tRNA of the invention is advantageously used ***to insert essentially any amino acid, whether natural or artificial,*** into a growing polypeptide, during translation, in response to a selector codon.

Thus the suppressor tRNA taught by Thorbjarnardottir et al clearly anticipates the generic O-tRNA of claim 1 or claim 17. Furthermore the tRNA<sup>Leu</sup> sequence shown on page 220, fig. 1 comprising a sequence comprising an anticodon loop comprising a CU(X)<sub>42</sub> **CTAAA** sequence (the CTA in bold and underlined binds to the suppressor codon) which fulfills the structure recited in claims 1 and 17 (see positions 61-105 of sequence). The requirement for restriction among the Leu-ORS sequences of SEQ ID NO: 15 and 16 will be treated as an election of species. Thus the restriction requirement is appropriate and is made **FINAL**.

### ***Priority***

Acknowledgment is made to this application which is a national phase entry in the United States under 35 U.S.C. § 371 from International Application Number PCT/US20041022061, which has an international filing date of July 7, 2004 claims benefit of priority from U.S. Provisional Patent Application USSN 601485,451, filed July 7, 2003; and to Provisional Patent Application USSN 601488,215, filed July 16, 2003.

***Information Disclosure Statement***

The information disclosure statement filed on October 09, 2007 and September 13, 2007 for which a copy of the patent publication has been submitted in this application has been considered as shown by the Examiners signature next to each reference.

***Oath/Declaration***

The oath or declaration submitted on January 05, 2006 has been reviewed and is in compliance with 37 CFR 1.56.

***Drawings***

The drawings were received on January 05, 2006. These drawings are accepted.

***Specification***

This application contains sequence disclosures at page 67 table 1, that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, the specification fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below: Nucleic acid sequences of 10 or more nucleotides and amino acid sequences of 4 or more residues need to be designated with a sequence identifier. Wherein attention is directed to paragraph(s) §1.82 (c) and (e). Although an examination of this application on the merits can proceed without prior compliance, compliance with the Sequence Rules is required for the response to this Office action to be complete.

Examiner would like to point out that there is no information with regards to SEQ ID NO: of the nucleic acid sequences present on page 17, in the Brief Description of the Drawings for the mentioned in fig. 4 and 5. If the Drawings contain amino acid sequences that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2) then the Brief Description of the Drawings needs to state the SEQ ID NO: for the nucleotide and/or amino acid sequences. Unless the appropriate SEQ ID NO: accompanies the nucleotide and/or amino acid sequences in the actual Drawing sheet.

Furthermore the disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code in paragraphs [0159]. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. See M.P.E.P. § 707.05(e) for the acceptable notation of an Internet address. Correction is required.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 17-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 17-26 are rejected for the recitation: "...at least about..." The metes and bounds of this term are unclear. Clarification is required.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 17-26 are rejected under 35 U.S.C. 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 17-26 are drawn to a cell comprising a translation system that comprises a genus of orthogonal leucyl-tRNAs (leu-O-tRNAs) comprising a  $CU(X)_nXXXAA$  sequence and at least 25% suppressor activity in the presence of any cognate synthetase (claim 17) or a cell comprising a translation system comprising one leu-O-tRNAs from the group selected from SEQ ID NOs: 3, 6, 7, 12 or any leu-O-tRNAs derived from *Halobacterium* sp NRRC-1 and the Leucyl-orthogonal tRNA synthetase (Leu-O-tRS) of SEQ ID NO: 15 or any conservative variant thereof (claims 17-26).

Claim 19 recites “50% suppressor efficiency” and “cognate synthetase”. However while the Leu-O-tRNA were described by structure and function (as SEQ ID NOs: 3, 6, 7 and 12), the structure of the specific cognate synthetase to be used with any of the above Leu-O-tRNA are not described. Given that each orthogonal pair must be determined empirically, and that there is no common structure upon which one of skill in the art can rely to envision other species in the genus, applicants are not in

possession of the genus encompassed in the claims.

The Court of Appeals for the Federal Circuit has recently held that a “written description of an invention involving a chemical genus, like a description of a chemical species, ‘requires a precise definition, such as be structure, formula [or] chemical name,’ of the claimed subject matter sufficient to distinguish it from other materials.” *University of California v. Eli Lilly and Co.*, 1997 U.S. App. LEXIS 18221, at \*23, quoting *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these.

However, according to the definition in the specification, the term ‘conservative variant’ encompasses sequences with 50% identity to SEQ ID NO: 15. The specification does not teach a structure/function correlation for any Leu-O-tRS sequence with up to 50% variation while retaining suppressor efficiency. Thus the specification does not convey to the skilled artisan that Applicants were in possession of the claimed genus of Leu-ORS variants or cognate synthetases that can suppress a suppressor codon with at least 50% efficiency.



In the instant specification, all of the disclosed species of leu-ORS and/or leu-O-tRNA pairs are empirically identified using a screening procedure. However this screening procedure does not provide the required description for the claimed genus of orthogonal pairs encompassed in the claimed translation system in the cell.

Given this lack of description of representative species encompassed by the genus of the claim, the specification does not sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 17, 23-26 rejected under 35 U.S.C. 102(b) as being anticipated by Thorbjarnardottir et al (in IDS). Thorbjarnardottir et al teach cloning and sequencing of a leucyl tRNA from *E. coli* that suppresses an amber codon comprising an anticodon sequence comprising CU(X)<sub>n</sub> XXXAA and G28:C42 and G49:C65 sequence. M 13 phage carrying two amber mutations were able to grow when these phages also carry the suppressor tRNA<sup>leu</sup>. Thorbjarnardottir et al on page 220, fig. 1 show a tRNA<sup>leu</sup> with

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an anticodon sequence CU(X)<sub>42</sub> CTAAA (see positions 61-105 of sequence) wherein said sequence comprises the suppressor codon. No correlation between any specific structure and 25% suppression activity is provided in claims 17 Applicant's claim. Therefore because Thorbjarnardottir et al's suppressor tRNA<sup>leu</sup> allows growth of phage M 13 carrying two amber codons the suppressor mutant would have at least a 25% suppressor activity thus would anticipate claims 17, 23-26. Claim 26 is anticipated because the structures of the O-tRNA and O-RS are not disclosed. The term derivative is defined as a molecule made from a specified molecule or information from a specified molecule or organism. Thus although the molecules can be isolated from *Halobacterium* sp *NRC-1* or from *Methanobacterium thermoautotrophicum*, other sequences comprising undisclosed number of residues are not excluded.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 17-26 are rejected under 35 U.S.C. 102(e) as being anticipated by WO/2002/085923 Schultz et al (in IDS). The specification and the claims (claims 1-7, 10 and 11) in Schultz et al teach a cell comprising an orthogonal tRNA that recognizes a selector codon in the presence of an ORS. Claim 10 in Schultz et al (WO/2002/085923)

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teaches an O-tRNA (SEQ ID NO: 3) that is 100% identical to the leu-O-tRNA of SEQ ID NO: 3. Furthermore claim 11 in (WO/2002/085923 Schultz et al) teaches an O-RS of SEQ ID NO: 65 that shows 100% identity to the leu-O-RS of SEQ ID NO: 15 claimed in instant claim 18. While the claims are not recited identically, the teachings in Schultz et al encompass cells comprising a genus of O-tRNA/O-RS pairs, and identical species of O-tRNA/O-RS pairs that are claimed in the instant application. Claim 10 in WO/2002/085923 Schultz et al teaches the identical structure of SEQ ID NO: 3. Claim 11 teaches SEQ ID NO: 65 that is identical to SEQ ID NO: 15.

The applied reference has a common inventors with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Claims 17-19, 21, 22-26 are rejected under 35 U.S.C. 102(e) as being anticipated by US PAT 7,083,970 B2 Schultz et al. Schultz et al teach compositions comprising an orthogonal tRNA<sup>leu</sup> derived from five different archael Leucyl tRNAs for which the anticodon was replaced with amber suppressor codons. Among the OtRNA<sup>leu</sup> disclosed, the OtRNA<sup>leu</sup> of SEQ ID NO: 2 shows 100% identity to the OtRNA<sup>leu</sup> of SEQ ID NO: 3 in the present application. The OtRNA of SEQ ID NO: 2 also comprises the anticodon loop comprising CU(X)nXXXAA sequence, and would be expected to have at

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least about a 25% suppression activity by virtue of having an identical structure to SEQ ID NO: 3. The OtRNA<sup>leu</sup> of SEQ ID NO: 2 in Schultz et al also comprises: A stem region with the discriminator base at position 73, comprises a C:G base pair at position 3:70 suppress an amber codon when used with an ORS<sup>leu</sup> (claim 17-19). Furthermore Schultz et al use an OtRNA<sup>leu</sup> derived from Halobacterium and the ORS<sup>leu</sup> derived from Methanobacterium thermoautotrophicum to suppress the [3-1actamase reporter gene comprising an amber codon in E. coli (claims 21, 23-26).

**Conclusion:** No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KAGNEW H. GEBREYESUS whose telephone number is (571)272-2937. The examiner can normally be reached on 8:30am-5:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Kagnew H Gebreyesus PhD  
Examiner  
Art Unit 1656

/Robert B Mondesi/  
Primary Examiner, Art Unit 1652